

### REMARKS

Claims 107, 113, 120-125, 131-137, 147, 228 and 230 have been cancelled in this amendment. Claims 104, 108, 119, 144, 148, 225, 229, 231, 232 and 236-238 have been amended in this amendment. Claims 239-268 have been added. No new matter has been added.

#### Claims 104-106, 108 and 119

The Examiner stated that previously pending claim 113, which depended from claim 104 and specified that the fungus is *A. terreus*, would be allowable if rewritten as an independent claim incorporating the limitations of the claims from which it depended. Claim 104 has been amended to incorporate the limitations of previously pending claim 113. Thus, claim 104 now specifies *A. terreus* and is believed allowable. Claims 105, 106, 108 and 119 depend from claim 104 and are believed to be allowable.

#### Claims 225-227, 229 and 231

The Examiner stated that previously pending claim 230, which depended from claim 225 and specified that the fungus is *A. terreus*, would be allowable if rewritten as an independent claim incorporating the limitations of the claims from which it depended. Claim 225 has been amended to incorporate the limitations of claim 230. Thus, claim 225 now specifies *A. terreus*. Claims 226, 227, 229 and 231 depend from claim 225 and are believed to be allowable.

#### Claims 237 and 238

Claims 237 and 238 depend, in the alternative, from claims 104 and 225 and are believed to be allowable.

#### Rejections Under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 144-148 and 232-236 under 35 U.S.C. §112, first paragraph as not enabled. The Examiner stated that the claims require "polyketides to be

'produced' rather than simply modulated." The Examiner argued that these claims are not enabled because increased expression of CreA decreases the expression of some polyketides.

#### **Methods for producing a polyketide**

Claims 144-146, 148 and 232-234 and 236 have been amended to specify *A. terreus*. Claims 147 and 235 have been cancelled. New claims 247-256 are drawn to a method for producing a polyketide. These claims specify either: the use of "a fungus that produces the polyketide and has been genetically modified to overexpress CreA" (claims 247-251) or the use of "a fungus that produces the polyketide and has been genetically modified to conditionally express CreA" (claims 252-256). Thus, claims require that the fungus produce the polyketide irrespective of the overexpression or conditional expression of CreA. Moreover, although the declaration data indicate that the production of some polyketides, e.g., erdin, is decreased upon overexpression of CreA, the declaration does not indicate that CreA overexpression or CreA conditional expression eliminates the production of any of the polyketides examined. In each case the polyketide is produced, meeting the limitations of the claims. There is nothing in the claims requiring that the expression of any particular polyketide be increased. The only requirement is that the polyketide be produced. In view of this, Applicants submit that claims 247-256 are enabled.

#### **Methods for producing a statin**

New claims 239-246 are drawn to a method for producing a statin. These claims specify the use of "a fungus that produces the statin and has been genetically modified to overexpress CreA" (claims 239-242) or "a fungus that produces the statin and has been genetically modified to conditionally express CreA" (claims 243-246).

The Declaration of Edward Driggers Under 37 C.F.R. §1.132 (previously submitted) included data regarding the effect of CreA overexpression on the production of five different polyketides in the statin pathway. The production of each of these five polyketide was increased when CreA was overexpressed. Thus, there is no basis for suggesting that claims drawn to a

method for producing a statin using a fungus that produce the statin has been genetically modified to overexpress (or conditionally express) CreA are not enabled.

Rejections Under 35 U.S.C. §102(b)

The Examiner rejected claims 104-108, 119, 144-147, 225-229, 231-235, 237 and 238 under 35 U.S.C. §102(b) as anticipated by Fillinger et al. (*FEBS Letters* 368:547, 1995).

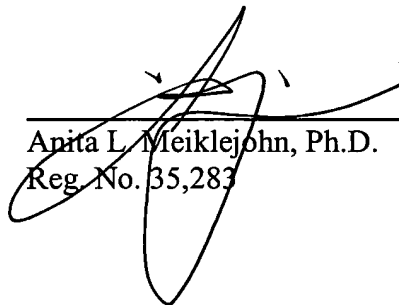
Fillinger et al. describes the overexpression of CreA in *A. nidulans*. The Examiner argued that "absent any evidence to the contrary, the host cell must necessarily produce/modulate the production of lovastatin, as well as a number of other polyketides such a mevinolin and monacolin, thereby anticipating the claimed methods.

Claims 104-108, 119, 144-147, 225-229, 231-235, 237 and 238 have been amended to recite *A. terreus* or have been cancelled. New claims 257-268 are drawn to methods which include "isolating a fraction of culture medium containing the polyketide." Applicants take no position regarding whether the modified *A. nidulans* of Fillinger et al. inherently modulate the production of or produce any particular polyketide. However, nothing in Fillinger et al. teaches or suggests culturing the modified *A. nidulans* and isolating a fraction of culture medium. Thus, Fillinger et al. cannot anticipate any of claims 257-268.

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Respectfully submitted,

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